Novel biomarkers of arterial and venous ischemia in microvascular flaps.

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Public Summary:

We demonstrate for the first time, differences in the gene expression of rat superficial inferior epigastric flaps undergoing arterial ischemia and venous congestion. Further, we have identified a large list of differentially expressed genes for the two types of vascular insults. These results offer insight into the mechanistic pathway of flap failure, and may be relevant to the pathogenesis in human flaps.

Scientific Abstract:

The field of reconstructive microsurgery is experiencing tremendous growth, as evidenced by recent advances in face and hand transplantation, lower limb salvage after trauma, and breast reconstruction. Common to all of these procedures is the creation of a nutrient vascular supply by microsurgical anastomosis between a single artery and vein. Complications related to occluded arterial inflow and obstructed venous outflow are not uncommon, and can result in irreversible tissue injury, necrosis, and flap loss. At times, these complications are challenging to clinically determine. Since early intervention with return to the operating room to re-establish arterial inflow or venous outflow is key to flap salvage, the accurate diagnosis of early stage complications is essential. To date, there are no biochemical markers or serum assays that can predict these complications. In this study, we utilized a rat model of flap ischemia in order to identify the transcriptional signatures of venous congestion and arterial ischemia. We found that the critical ischemia time for the superficial inferior epigastric fasciocutaneus flap was four hours and therefore performed detailed analyses at this time point. Histolgical analysis confirmed significant differences between arterial and venous ischemia. The transcriptome of ischemic, congested, and control flap tissues was deciphered by performing Affymetrix microarray analysis and verified by qRT-PCR. Principal component analysis revealed that arterial ischemia and venous congestion were characterized by distinct transcriptomes. Arterial ischemia and venous congestion was characterized by 408 and 1536>2-fold differentially expressed genes, respectively. qRT-PCR was used to identify five candidate genes Prol1, Muc1, Fcnb, Il1b, and Vcsa1 to serve as biomarkers for flap failure in both arterial ischemia and venous congestion. Our data suggests that Prol1 and Vcsa1 may be specific indicators of venous congestion and allow clinicians to both diagnose and successfully treat microvascular complications before irreversible tissue damage and flap loss occurs.

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